REMARKS

Reconsideration and allowance of the subject application are requested.

Applicants first thank the Examiner for the courtesies extended to applicants' representative during the telephone discussion on March 19, 2003.

Claim 28 is amended above to specify that expression of both G1 glycoprotein and G2 glycoprotein is effective to confer protective immunity against Hantavirus infection. Support for this revision is found throughout the original disclosure, for instance, in the examples section. No new matter is introduced by this amendatory language. Entry into the record of the amended claim is requested.

In the November 4, 2002 Office Action, the Examiner indicated that the subject matter of claims 33, 34, 42, 43, 50 and 51 is allowable.

In the March 5, 2003 Advisory Action, the Examiner indicated that the Amendment we filed on February 10, 2003 is entered.

However, claims 28-32, 35-41, 44, 45, 48 and 49 are rejected under 35 U.S.C. §103(a), as obvious over the combination of the following five references: (1) Schmaljohn (Rev. Med. Virol., 4:185-196, 1994); (2) Chu et al., (J. Virol., 69(10):6417-6423, 10/95); (3) Arikawa et al., (Virol, 176:114-125, 1990); (4) Montgomery et al., (Pharmacol. Ther., 74(2):195-205, 1997); and (5) Donnelly et al., (Ann. Rev. Immunol., 15:617-648, 1997). We respectfully disagree with the Examiner for the following reasons.

In response to our Amendment filed August 16, 2002, the Examiner first stated that independent claim 28 does not specifically recite a "vaccine", but a "composition", which is allegedly not commensurate in scope with the arguments we presented in that Amendment. In our February 10, 2003 Amendment, this claim was amended to recite that the composition confers protective immunity against Hantavirus infection. This makes the effectiveness of the composition to confer protective immunity a necessary requirement. In the amendments above, we have further amended claim 28 to specify that expression of both G1 glycoprotein and G2 glycoprotein is effective to confer protective immunity against Hantavirus infection. These two amendments are believed to clearly distinguish our invention from anything taught or suggested by any of the cited

references, which as noted by the Examiner during the March 19, 2003 telephone discussion, at best teach the use of G1 or G2 individually but not together.

In addition, as suggested by the Examiner on March 19, we append here a signed Rule 132 Declaration providing data that both G1 and G2 glycoproteins are needed to confer protective immunity, and that just one alone is insufficient. In light of the teachings of the cited art, this represents unexpected results achieved by the use and practice of the invention. The data includes a comparison study of G1 and G2, used alone and together.

In particular, Table 1 provides evidence that DNA vaccines expressing G1 or G2 alone fail to elicit neutralizing antibody responses and fail to protect against hantavirus infection. The inventors postulated that if G1 or G2 alone was sufficient to confer protective immunity, then this would make the development of a multivalent hantavirus DNA vaccine less complex. To test the hypothesis that a DNA vaccine expressing either G1 alone or G2 alone could confer protective immunity, hamsters were vaccinated 3-4 times with DNA vaccine plasmids expressing only the Hantaan virus G2 protein or only the Hantaan G1. Sera from vaccinated hamsters were tested for neutralizing antibodies using a plaque reduction neutralization test. Vaccinated hamsters were challenged with Hantaan virus. Four weeks after challenge sera was collected and assayed for the presence of anti-nucleocapsid antibodies, which serve as surrogate markers for evidence of Hantann virus infection. None of the hamsters vaccinated with plasmids expressing a single glycoprotein elicited neutralizing antibodies and the levels of protection were no greater than negative controls (see Table 1). Therefore, DNA vaccination with plasmids expressing either G1 or G2 is insufficient to confer protective immunity.

However, as shown in Tables 2 and 3, the particle mediated epidermal delivery (PMED), or gene gun, vaccine provides, with certain exceptions (e.g., there is not necessarily 100% protection against the homotypic virus, and not all heterotypic viruses, such as Puumala, virus are protected against) homotypic and heterotypic protection of hamsters to challenge with virus.[1] For instance, homotypic protection is clearly evident

[1] "Homotypic" refers to the same subtype of virus used in the vaccine or immunogenic composition, and "heterotypic" refers to a different subtype of virus. For example, the Hantaan DNA vaccine protects against the homotypic virus (Hantaan virus), and against some heterotypic viruses (e.g., Dobrova virus and

in vaccines employing either Seoul or Hantaan virus M gene-based DNA vaccines, albeit reduced, when compared to homotypic vaccination and challenge. Thus, DNA vaccine compositions expressing both G1 and G2 are effective in conferring protective immunity against Hantavirus infection.

We believe this provides the Examiner with the evidence that clearly distinguishes our claimed invention from any of the cited references, taken alone or in combination with each other. In summary then, the combined disclosures of Schmaljohn, Chu, Arikawa, Montgomery and Donnelly to arrive at the compositions and methods of our claimed invention. Therefore, we submit that none of claims 28-32, 35-41, 44, 45, 48 and 49 would have been obvious at the time of our invention, in light of the five references cited by the Examiner. Reconsideration and withdrawal of this rejection is requested.

Having addressed all of the Examiner's outstanding concerns, it is believed that this application is in condition for allowance, and notice of such is earnestly solicited. No amendment made was related to the statutory requirements of patentability unless expressly stated herein, and no amendment made was for the purpose of narrowing the scope of any claim unless we argued above that such amendment was made to distinguish over a particular reference or combination of references.

If the Examiner has any questions or would like to make suggestions as to claim language, he is encouraged to contact Marlana K. Titus at (301) 762-8214.

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Seoul virus). In the art, the terms "homologous" and "heterologous" can be used interchangeably with "homotypic" and "heterotypic".

MARKED-UP VERSION OF THE CLAIMS AS AMENDED ABOVE

Please amend claim 28 as follows.

28. (Twice Amended) A composition that confers protective immunity against Hantavirus infection, comprising

(c) an inert particle suitable for carrying a polynucleotide stably coated thereon, and

(d) a polynucleotide coated onto the particle, which polynucleotide comprises a promoter operative in a mammalian cell and a hantavirus M gene segment encoding a G1 glycoprotein and a G2 glycoprotein,

wherein expression of both G1 glycoprotein and G2 glycoprotein is effective to confer protective immunity against Hantavirus infection.